AETIOLOGICAL DIAGNOSIS

IN PLEURAL EFFUSION

Dissertation submitted to Coimbatore Medical College for

M.D. Degree in General Medicine

Branch I

The TamilNadu

Dr.M.G.R. Medical University

Chennai

September 2006

CERTIFICATE

This is to certify that the enclosed work **"ETIOLOGICAL DIAGNOSIS OF PLEURAL EFFUSION IN HUNDRED CASES"** submitted by Dr. K. BABURAJ to The Tamilnadu Dr. M.G.R. Medical University is based on bonafide cases studied and analysed by the candidate at the Department of Medicine, Coimbatore Medical College Hospital during the period from January 2004-December 2005 under my guidance and supervision and the conclusions reached in this study are his own.

Prof. Of Medicine
Unit Chief

Prof. And Head
Of
Department Of Medicine

Dean

DECLARATION

I solemnly declare that the dissertation titled **"ETIOLOGICAL DIAGNOSIS OF PLEURAL EFFUSION IN HUNDRED CASES"** was done by me at **Coimbatore Medical College Hospital** during the period from January 2003 – December 2005 under the guidance and supervision of Professor **Dr.S. PRABHA**, M.D.

This dissertation is submitted to the TamilNadu Dr. M.G.R. Medical University towards the partial fulfillment of the requirement for the award of **M.D. Degree** (Branch – I) in **General Medicine.**

Place:

Date: **Dr. K. BABURAJ**

ACKNOWLEDGEMENT

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I thank **Dr. T.P. KALANITI**, M.D., our beloved Dean, for permitting me to conduct the study in this hospital.

I am thankful to **Dr. G. YASODHARA**, M.D., Professor and Head of the Department of Medicine for her advice and encouragement, given for this study.

I am deeply indepted to **Dr.S.PRABHA**, M.D., Professor of Medicine, our Unit Chief for his valuable advice and guidance.

I am grateful to **Dr. R.K.GEETHA**, DCP., M.D., Head of the Department of Microbiology, **Dr.Rengaramani**.M.D .,Head of the department of Bio-Chemistry and **Dr.Indirapranesh.**M.D ., Head of the department of Pathology for allowing me to make use of the various investigation facilities.

I also acknowledge the assistance rendered by **Dr.K. GOVINDARAJ**,M.D,D.M., **Dr.RAMKUMAR**, M.D, DTCD. And **Dr.Sudalaimuthu**,DMRD for their valuable advice and guidance throughout this study.

I thank **Dr.S.AVUDAIAPPAN**, M.D., **Dr. P.S.RANI**, M.D., **Dr.SELVARAJ** and **Dr. T.CHAKRAVARTHY,** M.D., our Assistant Professors for their advice and guidance.

I sincerely thank all the patients and their family members for their whole-hearted co-operation and patience without which this work would not have been possible.

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INTRODUCTION

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Pleural Effusion is an accumulation of fluid in the pleural space as a result of excessive transudation or exudation from the pleural space. It is a sign of disease and not a diagnosis itself.

Whenever an adjacent organ is infected, the sympathetic pleura sheds its tear into the pleural space, the accumulation which is encountered by the clinician frequently as a serious manifestation of thoracic disease, pulmonary or cardiac and occasionally as the first evidence of some other profound systemic disease.

The advancements in the field of medicine, the advent of newer antibiotics and various diagnostic aids like pleural fluid analysis, pleural fluid cytology, Pleural Biopsy, ultrasonography, bronchoscopy, aspiration of scalene lymph node, serological test for ANA, ADA, rheumatoid factor, pleural fluid amylase and CT- thorax helps the Physician to arrive at a correct Diagnosis in the early course of the disease.

I report here a preliminary study of hundred (100) cases of pleural effusion considering the importance of early Diagnosis and management.

AIM OF THE STUDY

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1. To Find out the Etiological diagnosis of Pleural Effusion in **Hundred Cases** (100 cases) admitted in CMC Hospital between 2003 – 2006

2. To find out the incidence of pleural effusion in different age groups.

3. To find out rare causes of pleural effusion.

REVIEW OF LITERATURE

PLEURAL EFFUSION

DEFINITION

Pleural effusion is the result of the accumulation of fluid in the pleural space, are a common medical problem[59]. They can be caused by several mechanisms including increased permeability of the pleural membrane, increased pulmonary capillary pressure, decreased negative intrapleural pressure, decreased oncotic pressure, and obstructed lymphatic flow Pleural effusions indicate the presence of disease which may be pulmonary, pleural, or extra pulmonary.

In the course of embryological development the pleural membrane is formed from mesenchyme to line the space that will separate the lungs from mediastinum, diaphragm and chest wall.[59]

NORMAL COMPOSITION OF PLEURAL FLUID[60]

VOLUME	-	0.1 -- 0.2 ml/Kg
Cells/mm.cu	-	1000 - 5000
% mesothelial cells	-	3 – 70%
% macrophages	-	30 – 75%
% lymphocytes	-	2 – 30%
% granulocytes	-	10 %
% albumin	-	~ plasma level
Protein	-	1 – 2 gm/dl
Glucose	-	< 50 % plasma level
LDH	-	> plasma level
Ph	-	> plasma level

1) ANATOMY OF PLEURA: [61, 62]

Each lung is invested by a delicate serous membrane which is arranged in the form of a closed invaginated sac and is termed the pleura. The portion which covers the surface if the lung and lines the tissues in-between its lobes is called the visceral pleura. The rest of the membrane lines the inner half of the chest wall, covers a large part of the diaphragm and is reflected over the structures occupying the middle part of the thorax is termed the parietal pleura. The visceral and parietal pleura are continuous with each other around and below the root of the lung. In healthy they are in actual contact with each other in all phases of respiration, the potential space between them is called the pleural cavity.

The interval in-between two sacs is called interpleural space or mediastinum. The right pleural cavity is wider than the left because the heart extends further to the left than to the right. The pleuron covers the apices of the lung 1 inch above the medial third of the clavicle. The anterior margin found to converge, as they pass behind the sternoclavicular joints and come into apposition at the lower border of the manubrium sterni. It may be noticed that the anterior margin remains in apposition upto the level of the 4^{th} costal cartilage. Right pleura continues vertically, but the left arches out and descend lateral to the border of the sternum, half way to the apex of the heart. Each turns laterally at the 6^{th} costal cartilage and passing around the chest wall crosses the mid-clavicular line at the 8^{th} rib and the mid-axillary line at the 10^{th} rib. This lower border is the costo-phrenic recess; it falls somewhat short of the costal margin between the sternum

and the mid-axillary line. It crosses the 12th rib at the lower border of the sacro spinalis muscle and passes in horizontally to the lower border of the 12th thoracic vertebra.

The arterial supply and lymphatic drainage of the parietal pleura are intercostals, internal thoracic and musculo-phrenic arteries and nodes respectively. The nerve supply is from the intercostals and phrenic nerves. The arterial supply of the visceral pleura is by the branches of the pulmonary arteries and the capillaries drain into both systemic and pulmonary venous system. Its lymphatics join with those of the lungs and the nerve supply is derived from the autonomic system (vasomotor supply). It is insensitive to ordinary stimuli.

2) PHYSIOLOGY OF THE PLEURA: [63]

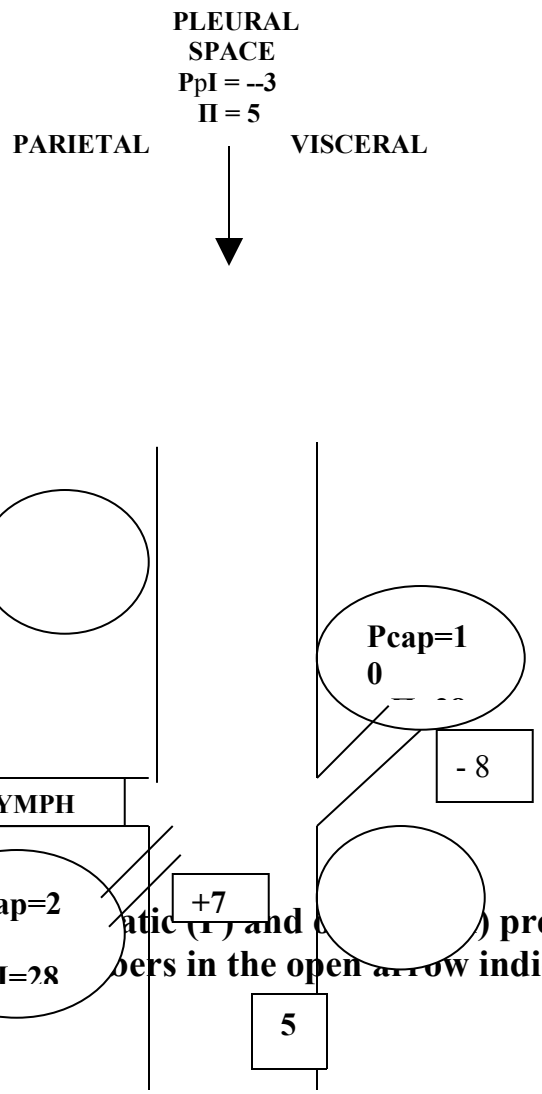


Fig 1. Distributi atic (1) and) pressure across the parietal and visceral pleu bers in the open arrow indicate the net magnitude of

the pressure differences that promote filtration and reabsorption across the parietal and visceral pleura respectively.

[63, 64]During normal respiration there is negative pressure in relation to the atmosphere (about -0.66kpa at functio0nal residual capacity) within the pleural space. This would trend to suck capillary fluid and gas from the surrounding tissue into the spaces if it were not for other balancing factor. The pleura transmits the force generated by the respiratory muscles of the lung[65] There s a regular transfer of low protein fluid from parietal to pleural space. Protein and particles are turned over much less rapidly, being absorbed by lymphatic vessels opening into the parietal pleura.[64, 66, 67, 68]

Pleural liquid pressure:

Pleural surface pressure increased approximately 0.5 cms of H2O of vertical distance from the apex to the base of the lung.[65] The pleural fluid is in a dynamic state 30 – 75% of water being turned over every Hr on normal respiration.[66, 67]

Pleural space is lubricated by a thin film of serous fluid, few milliliter of fluid from the normal space. For this lubrication surfactant would be more effective, have been identified in the pleural fluid.[68, 69]

3) PATHOPHYSIOLOGY: [70]

Normal interstitial fluid is filtered from the arterial end of the capillary, upto 90% is reabsorbed at the venous part of the capillary bed and the rest is removed by the lymphatics. Three main factors involved in the fluid movement are:

1) Capillary Permeability
2) Hydrostatic Pressure
3) Colloid Osmotic Pressure

The potential pleural spacer has very close proximity to both the systemic and pulmonary circulation. Thus, the parietal pleura is supplied by the systemic circulations via, the intercostals arteries and its venous drainage is mainly through the azygos systems into the superior venacava.

In contrast, the arterial supply of the visceral pleura is by branches of the pulmonary artery and their capillaries drain into both systemic and pulmonary venous system. The intravascular hydrostatic pressure within the venous end of the visceral pleural capillaries is less than hydrostatic pressure in the capillaries of the parietal pleura. Thus, considering the pleural surfaces in isolation, the two separate circulatory systems could presumably cope with filtrate, however, because of their closer proximity the visceral pleura ifs able to apply a sucking force to the pleural space which not only keeps the later virtually free of fluid but also keeps the visceral and parietal surfaces apposed against the forces of lung elastic recoil inwards and the chest wall outwards.

The visceral pleural capillary bed has a large capacity to absorb protein-free fluid. Protein removal is by the lymphatic system. Normally, the pleural space contains small amount of fluid low in protein content but in pleural effusion the later is increased. However, the capacity of the lymphatic system to deal with protein is small.

The factors influencing pleural fluid transport have been reviewed in detail by Black (1972). When equilibrium between formation and absorption of pleural fluid is upset to either one of the following reasons, abnormal accumulation of pleural fluid occurs.

MECHANISM THAT LEADS TO ACCUMULATION OF PLEURAL FLUID:[70, 71]

1) Increased hydrostatic pressure in the microvascular circulation (CCF).
2) Decreased oncotic pressure in the microvascular circulation (hypoalbuminemia)
3) Decreased pressure in the pleural space (complete lung collapse)
4) Increased permeability of the microvascular circulation (pneumonia)
5) Decreased lymphatic drainage from the pleural space (malignancy)
6) Movement of fluid from the peritoneum (ascites)

Small pleural tumor implants are common pathological findings. Such metastasis can cause capillary and lymphatic obstruction and obliteration resulting in increasing pleural fluid production and decreased resorption. In addition secondary infection, association either with the primary tumor in the case of lung cancer or with metastasis, results in further inflammation and increased capillary permeability. Occasionally erosion of small vessels by tumor implants may cause hemorrhage into the pleural space.

Major Mediastinal lymph node involvement, which occurs commonly in lymphoma and small cell carcinoma of the bronchus, may interfere with lymphatic drainage and results in pleural effusion with negative cytology. Protein is unable to re-enter the vascular space and causes increase in pleural osmotic pressure and secondary accumulation if fluid. Obstruction of the superior venacava occurs with bronchial carcinoma and lymphoma. The elevation of systemic venous pressure causes a decrease in parietal pleural resorption and lymphatic flow.

4) PATHOGENESIS OF EFFUSION IN VARIOUS DISEASES: [72, 73]

Primary pathologic involvement of pleura is very rare. Primary disorders that are reasonably common are :

1) Primary intrapleural bacterial infections that imply seeding of space as an isolated focus in the course of a transient bacteremia.
2) A primary neoplasm of the pleura, a mesothelioma. Except these exception, usually pleural disease follow some underlying disorder, most often pulmonary and usually the pleural involvement is only an inconspicuous feature of the primary process. Secondary infections are extremely common, occasionally; secondary pleural disease assumes a dominant role in the clinical problem, as occurs in bacterial pneumonia, with development of empyema.

The disease of the pleura can be divided into

a) Inflammatory
b) Non - Inflammatory

Inflammation:

Inflammation of the pleura can be divided into the following according to the character of resultant exudates into serous, fibrinous, serofibrinous, suppurative and hemorrhagic pleuritis.

Serous, Fibrinous, Serofibrinous essentially caused by the same process the amount of fibrinous component depends largely on the stage and severity of inflammation. Common causes within the lungs are tuberculosis, pneumonia, pulmonary infarction, lung abscess, bronchiectasis, rheumatic fever, disseminated lupus

erythematosis, uremia, systemic infections like typhoid fever, tularemia, ornithosis, blastomycosis and coccidioidomycosis. Occasionally metastatic involvement of pleura can occur. The pleura is almost invariably affected by tuberculosis and the pleural reaction in the early stage tends top remain as a serous or copious serofibrinous exudation, commonly designated as pleurisy with effusion.

Suppurative pleuritis is designated as frank, purulent exudate usually implies bacterial or mycotic seeding of the pleural space. Rarely, suppurative infection of the pleura sometimes undergo thick, dense cartilaginous connective tissue layer is formed that envelopes the lungs and seriously embarrasses the pulmonary expansion. Calcification may occur in this scar tissue. Massive calcification is particularly characteristic of Tuberculous empyema.

Hemorrhagic pleuritis exudates are infrequent and are usually found only in hemorrhagic diathesis, rickettsial disease, malignancy and very rarely in tuberculosis.

Non- inflammatory pleural collection:

Hydrothorax is non- inflammatory collection of serous fluid within the pleural cavities. The most common cause of hydrothorax is congestive cardiac failure. Other conditions that produce transudative effusions are:

1) Renal failure

2) Liver disease, particularly cirrhosis of liver with ascites, it is generally believed that the fluid reaches the pleural cavity via, transdiaphragmatic lymphatics

3) Meig's syndrome- ovarian tumor (fi**10**) with ascites with right sided hydrothorax. Ti is now appreciated that any type of ovarian tumor may cause this syndrome.

Inmost instance hydrothorax is not loculated. If the underlying cause is alleviated hydrothorax may get reabsorbed. Usually leaving behind no permanent alteration.

Hemothorax is the escape of blood into the pleural cavity. It is almost invariably fatal complication of aortic aneurysm.

Chylothorax designates an accumulation of milky fluid, usually of lymphatic origin; chyle is milky white because it contains finely emulsified fats which should be differentiated from turbid serous fluid. It is most often encountered in malignancies arising within the thoracic cavity, which often cause obstruction to the major lymphatic ducts. However, more distant cancer metastasis via the lymphatics and grow within the right lymphatic or thoracic duct causing obstruction resulting in chylothorax. Less commonly it may accompany traumatic rupture or perforation of a lymphatic malignancy, is most commonly caused by obstruction or destruction of thoracic duct by lymphoma.

CAUSES OF A PLEURALEFFUSION

Pleural effusions are classified into transudates and exudates. A transudative pleural effusion occurs when the balance of hydrostatic forces influencing the formation and absorption of pleural fluid is altered to favour pleural fluid accumulation. The permeability of the capillaries to proteins is normal.[74] In contrast, an exudative pleural effusion develops when the pleural surface and/or the local capillary permeability are altered.[75] There are a multitude of causes of transudates and exudates

5) Etiology: [76]

1) Transudate-

A) Increased Hydrostatic Pressure:

- Left ventricular failure

B) Decreased Osmotic Pressure:

- Liver cirrhosis
- Hypoalbuminemia
- Peritoneal dialysis
- Hypothyroidism
- Nephrotic syndrome
- Mitral stenosis
- Pulmonary embolism
- Constrictive pericarditis
- Urinothorax
- Superior vena cava obstruction
- Ovarian hyperstimulation
- Meigs' syndrome

2) Exudative

A) Inflammatory Conditions of the Pleura:

- Tuberculosis
- Parapneumonic effusions(bacterial, viral, parasitic, Fungal)
- Pulmonary infarction
- Pulmonary embolism

B) Collagen vascular disease:

- Rheumatoid arthritis
- Autoimmune diseases(SLE)

C) Disorders of contagious structures:

- Esophageal rupture
- Diaphragmatic hernia
- Liver abscess
- Sub- phrenic abscess
- Pancreatitis

D) Malignancy:

- Malignancy of lung(primary and metastatic disease, Mediastinal and other lymph nodes)
- Mesothelioma

- Superior venacava obstruction

E) Rare causes:

- Post-myocardial infarction syndrome
- Yellow nail syndrome
- Drugs

Drugs known to cause pleural effusions

- Amiodarone
- Nitrofurantoin
- Phenytoin
- Methotrexate
- Carbamazepine
- Procainamide
- Propylthiouracil
- Penicillamine
- GCSF
- Cyclophosphamide
- Bromocriptine

- Benign asbestos effusion
- Post radiation therapy
- Uremia

Mycobacterium tuberculosis and pleural effusion: [77]

Character of the fluid:

Serous exudates, very rarely hemorrhagic.

Pathogenesis:

Most of the cases it spreads from underlying pulmonary focus. The effusion is always in the side of pulmonary lesion. Sometimes pleural effusion may be due to rupture of subpleural focus or pleural involvement in military tuberculosis.

Clinical features:

** 1/3 of patients will have acute illness less than one week duration.

** 2/3 will seek medical attention within a month, after the onset of sign (+) .

Symptoms:

** Common symptoms are –

Non- Productive cough

Pleuritic type if chest pain

Fever

50% may be febrile

Patients with chronic illness will have loss of weight, appetite, malaise and dyspnoea.

Tuberculous effusion is usually moderate and unilateral. In 1/3 of patients Tuberculous effusion will have co-existing parenchymal disease which is evident radiologically.

30% of patients with Tuberculosion will have negative tuberculin test. It will become positive after 8 weeks of development of symptoms.

Mycobacterium demonstrable in pleural fluid is only 10%. Culture will be positive in 25%. 50% cells in pleural fluid is mature lymphocytes. Eosinophil count rarely exceeds 10%.

HIV Infection: [2]

Pleural effusions are uncommon in such patients. The most common cause is Kaposi's sarcoma. Followed by parapneumonic effusion. Other common causes are tuberculosis, cryptococcosis and primary effusion lymphoma. Pleural effusions are very uncommon with pneumocystis carinii infection

Pancreatitis: [63]

Usually serous exudate but may be serosanguinous pleural fluid amylase higher than serum. Normal glucose, leucocytes 1000- 50,000 cells/mm.cu, polymorphs predominate, rarely eosinophils. Patient presents with history of acute abdominal pain, nausea, vomiting, rarely chest pain and dyspnoea. Usually pancreatic effusion is painless. 20% of patients with acute Pancreatitis will develop pleural effusion, usually left sided sometimes bilateral occasionally Right sided. Contact of the pleura with enzyme rich peripancreatic fluid through trans-diaphragmatic lymphatics and less through sinus tract between pancreatic pseudocyst and pleural space.

Diagnostics of pancreatic disease complicatio0ns based on the effusion's pancreatic enzyme activity, evaluation and visual methods such as computed tomography, ultrasonography, endoscopic retrograde cholangiopancreatography (ERCP).

Neoplasm: [70]

The exudates may be serous, serosanguinous or hemorrhagic. Obstructive pneumonitis with pleural effusion had very strong presumptive evidence per se for diagnosis. Recovery of cells from the pleural fluid or sputum, positive pleural biopsy, bronchoscopy or Mediastinal node biopsy, fine needle aspiration cytology (FNAC) of secondary lymph node or from metastatic secondaries.

Commonest cause of exudate more than age of 60 yrs. It is due to invasion of lung cancer into the pleura. Other causes are spread from liver metastasis and chest wall lymphatics in breast cancer. Very rarely ovarian and gastric cancer. 7% shows unknown primary. Mediastinal invasion with lymphatic blockage and effusion on the basis is suggestive of Hodgkins lymphoma.

Squamous cell carcinoma: [70]

This type is most commonly found in men. It is the form most closely correlated with a smoking history. The microscopic features are familiar in the form of production of keratin and intracellular ridges in the well-differentiated forms, but many less well-differentiated Squamous cell tumors are encountered, that beginning to merge with the undifferentiated large cell pattern. This tumor tends to metastasise locally and somewhat later than the other patterns, but its rate of growth in its site of origin is usually more than that of other types. Squamous metaplasia, epitheliod dysplasia and foci of frank carcinoma in situ are regularly present in [17] chial epithelium adjacent to the tumor mass.

Adenocarcinoma: [70]

Various classification of Adenocarcinoma include atleast two forms, the usual bronchial-derived Adenocarcinoma and bronchoalveolar carcinoma. The regular bronchial Adenocarcinoma occurs with equal frequency in both males and females. The lesions are usually more peripherally located, tend to be smaller and vary histologically from well- differentiated tumors with obvious glandular elements to papillary lesions resembling other papillary carcinomas, to solid masses with only occasional mucin – producing glands and cells. About 80% contains mucin when examined with mucin stain. Carcinoembryonic antigen will be elevated more than 10 ng /ml in specificity of 91.48% and sensitivity 87.5%. So Carcinoembryonic antigen (CEA) is useful to differentiate Adenocarcinoma from other neoplasms and that a positive result rules out mesothelioma.

Adenocarcinoma grows more slowly than Squamous cell carcinoma. It has been suggested that the Adenocarcinoma requires virtually 25 yrs to reach a size of 2 cms. Peripheral Adenocarcinoma are sometimes associated with area of scarring (scar carcinoma), but it may be difficult to determine whether the scar preceded or followed the cancer. Adenocarcinomas are less frequently associated with a history of smoking than Squamous cell carcinoma.

Papillary serous cystadenocarcinoma of the ovary:

Papillary serous cystadenocarcinoma of the ovary accounts for approximately 40% of all cancers of ovary. It occurs in later life, this tumor infiltrate the soft tissue and form large intraabdominal masses and rapid deterioration. The 5 yr survival rate and the tumor involving peritoneum is about 25%.

Empyema: [2]

Refers to a grossly purulent effusion.

Clinical features:

Pyrexia usually high remittent temperature with rigors, sweating, malaise and weight loss. Pleural pain associated with cough and sputum production. Pleural fluid cytology will be predominantly polymorphonuclear leucocytosis.

Organisms resulting in empyema thoracis:

	Gram (+ ve)
75% single organism	Streptococcus milleri
	Streptococcus pneumonia
	Staphylococcus aureus
	Gram (- ve)
	E.coli
	H.influenza
	Proteus
Anaerobic bacteria	B.melaninogenicus
	Fusobacterium
Fungi	candida. spp.
25% multiple organism	Streptococcus milleri + Anaerobes

Clinical Features:

The onset of symptoms depends upon the quantity of the effusion and the suddenness with which it appears. Pleuritic pain and dry cough are usually earliest

symptoms but there may be preceding period of fever, loss of appetite and loss of weight. When the effusion develops pain is often relieved. If the effusion accumulates rapidly dyspnoea, cyanosis and Mediastinal flutter may be evident.

Pleural effusion may be:

a) In general pleural space

b) Loculated ion the general pleural space

c) Interlobular

d) Infrapulmonary

Pleural effusion can be diagnosed clinically when the pleural fluid is more than 300 ml. And it can be

diagnosed radiologically in lateral view when it is 200 ml, in lateral Decubitus < 200ml and in PA view 500-600 ml.

If the effusion is in general pleural space and is sufficiently large the physical signs are:

1) Restriction of respiratory movements on the affected side

2) Stony dullness on percussion

3) Diminished or absent breath sounds

4) Diminished or absent vocal resonance and fremitus

5) Mediastinal displacement to the opposite side

Massive pleural effusion without Mediastinal shift suggests fixation of the mediastinum and the following possibilities should be considered:

a) Carcinoma of the main stem bronchus with atelectasis of the ipsilateral lung

b) Fixed mediastinum due to neoplastic lymph node

c) Malignant mesothelioma

d) Pronounced infiltration of the ipsilateral lung usually with fever.

At the upper level of the dullness, which sweeps upwards towards axilla, bronchial breathing may be heard. With small effusion the signs are best elicited at the base posteriorly. Effusion located within the fissures may not be detectable on physical examination, if there is no associated effusions in the general pleural space. Infrapulmonary effusion(subpulmonic effusion) may be clinically indistinguishable from fixed elevation of hemi-diaphragm with blunting of posterior costo-phrenic angle on lateral chest radiograph and other hint to diagnosis is widening of the distance between the top of the gastric bubble and the top of the Left hemi-diaphragm(2 cms). Also, an effusion on the Right side causes the minor fissure to appear close to the diaphragm than usual.

PHYSICAL SIGNS OF PLEURAL EFFUSION

Amount of Effusion	Expansion	Fremitus	Percussion	Breath Sounds	Contra lateral Mediastinal shift
Small effusion	N	N	N	V	0
300-1000 ml	Decreased	Decreased	F	Decreased **V**	0
1000-2000 ml	Moderately Decreased	Decreased	F	Moderately Decreased	+
>2000 ml	Severely Decreased	Moderately Decreased	F	Severely Diminished	++

N – Normal F – Stony Dullness V - Vesicular

O – Absent + - Present

MATERIALS AND METHODS

MATERIALS AND METHODS

100 cases of pleural effusion aged between 13 to 85 years who were admitted in the Coimbatore medical college hospital were taken up for investigation under the following heads:

LABORATORY INVESTIGATIONS:

1. Urine

- **Albumin**
- **Sugar**
- **Deposits**
- **24 hours urine protein**

2. Blood

- **TC**
- **DC**
- **ESR**
- **Hb gm%**
-

3. Blood

- **Urea**
- **Sugar**

4. Serum creatinine

5. Serum proteins

6. Mantoux

7. Sputum for AFB

8. Pleural fluid - culture

9. Pleural fluid - biochemical analysis

- **Protein**
- **Glucose**

10. Pleural fluid cytology

11. Chest X ray; PA / Lateral / Decubitus

12. Pleural biopsy

13. **Pleural fluid LDH / Serum fluid LDH**

14. **Pleural fluid amylase**

15. **ECG**

16. **Echocardiography**

17. **CT thorax / brain**

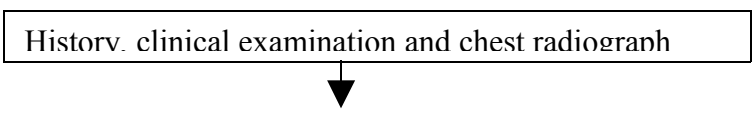
18. **FNAC**

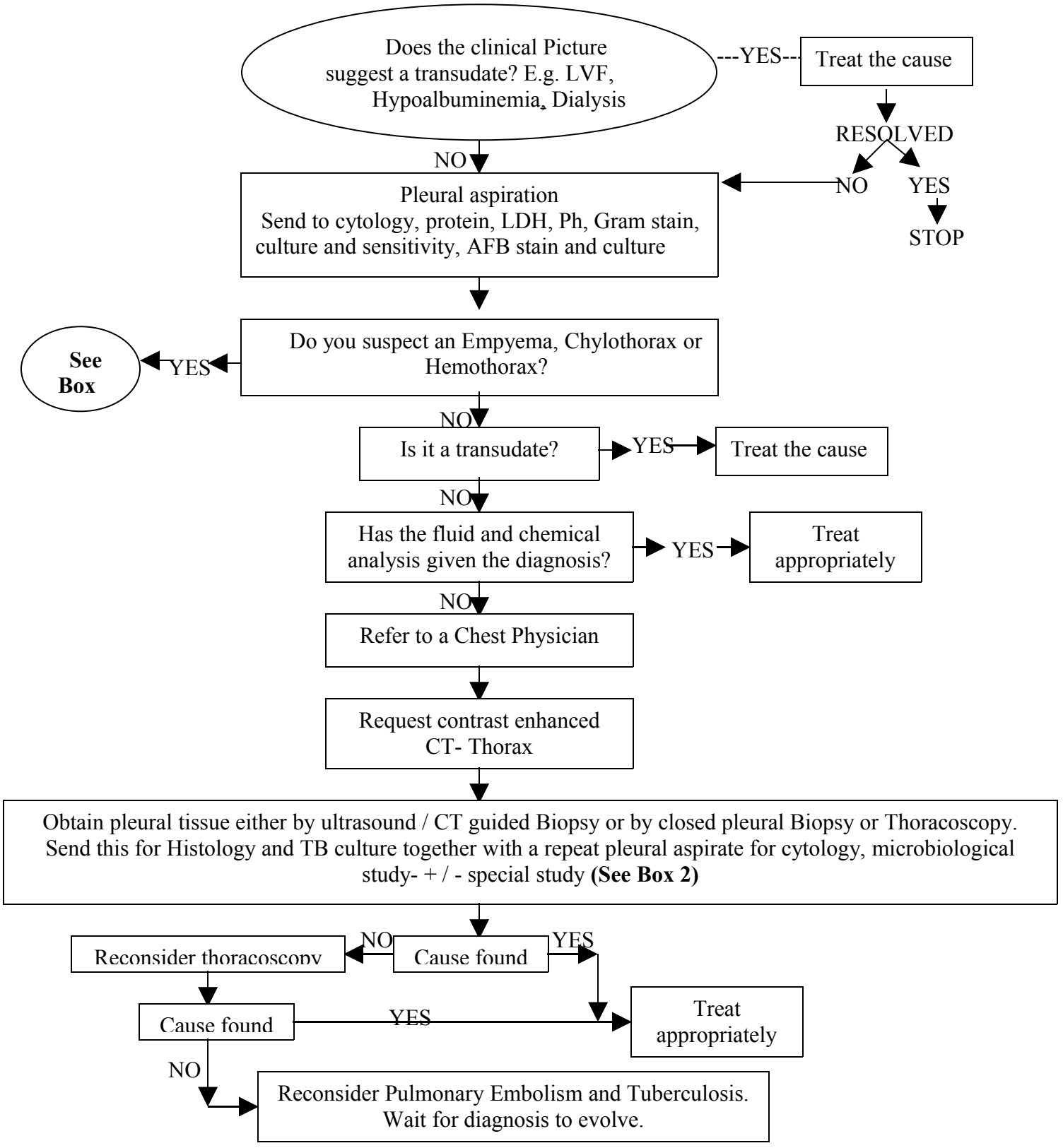
19. **ADA**

20. **ELISA for HIV**

21. **Others.**

Diagnostic Algorithm for investigation of pleural effusion[1]





Thorax 2003; 58(90002):8

Box 1: Additional Pleural Fluid Tests	
Suspected disease	**Tests**
Chylothorax	Cholesterol and Triglycerides
Hemothorax	Centrifuge Hematocrit
Empyema	Centrifuge
Box 2 : Pleural Fluid Tests Which May Be Useful In Certain Circumstances	
Suspected disease	**Tests**
Rheumatoid disease	Glucose Complement
Pancreatitis	Amylase

The initial step in assessing a pleural effusion is to ascertain whether it is a transudate or exudate. The biochemical analysis of pleural fluid is considered later Clinical assessment alone is often capable of identifying transudative effusions. Approximately 75% of patients with pulmonary embolism and pleural effusion have a history of Pleuritic pain. These effusions tend to occupy less than a third of the hemithorax and the dyspnoea is often out of proportion to its size. Approximately 75% of patients with

pulmonary embolism and pleural effusion have a history of Pleuritic pain.

The patient's drug history is also important.

RADIOLOGY:

The Most Sensitive Method of detection of pleural fluid is by Roentgenogram.

PA and lateral chest radiographs should be performed in the assessment of suspected pleural effusion.

The plain chest radiographic features of pleural effusion are usually characteristic. The PA chest radiograph is abnormal in the presence of about 200 ml pleural fluid. However, only 50 ml of pleural fluid can produce detectable posterior costophrenic angle blunting on a lateral chest radiograph.[4] Lateral decubitus films are occasionally useful as free fluid gravitates to the most dependent part of the chest wall, differentiating between pleural thickening and free fluid.[5]

Interlobar effusion may mimic tumor, occur partially in cardiac failure and their clearance following diuretic treatment has given rise to the term vanishing tumor.[6, 69] Subpulmonic effusions occur when pleural fluid accumulates in a subpulmonic location. They are often transudates and can be difficult to diagnose on the PA

radiograph and may require a lateral decubitus view or ultrasound. The PA radiograph will often show a lateral peaking of an apparently raised hemidiaphragm which has a steep lateral slope with gradual medial slope. The lateral radiograph may have a flat appearance of the posterior aspect of the hemidiaphragm with a steep downward slope at the major fissure.[5]

PLEURAL ASPIRATION (Thoracentesis):

A diagnostic pleural fluid sample should be gathered with a fine bore (21G) needle and a 50 ml syringe. The sample should be placed in both sterile vials and blood culture bottles and analysed for protein, lactate dehydrogenase (LDH, to clarify borderline protein values), pH, Gram stain, AAFB stain, cytology, and microbiological culture.

This is the primary means of evaluating pleural fluid and its findings are used to guide further investigation. Diagnostic taps are often performed in the clinic or by the bedside effusions often require radiological guidance. A green needle (21G) and 50 ml syringe are adequate for diagnostic pleural taps. The 50 ml sample should be split into three sterile pots to be sent directly for microbiological, biochemical, and cytological analysis.

Microscopic examination of Gram stained pleural fluid sediment is necessary for all fluids and particularly when a Parapneumonic effusion is suspected. If some of the microbiological specimen is sent in blood culture bottles the yield is greater, especially for anaerobic organisms.[6]

20 ml of pleural fluid is adequate for cytological examination and the fresher the sample when it arrives at the laboratory the better. If part of the sample has clotted, the cytologist must fix and section this and treat it as a histological section as it will increase the yield. Sending the cytology sample in a citrate bottle will prevent clots and is preferred by some cytologists. If delay is anticipated, the specimen can be stored at 4°C for up to 4 days.[7]

Percutaneous pleural biopsy:

Pleural tissue should always be sent for tuberculosis culture whenever a biopsy is performed.

In cases of mesothelioma, the biopsy site should be irradiated to stop biopsy site invasion by tumour.

When pleural biopsies are taken, they should be sent for both histological examination and culture to improve the diagnostic sensitivity for tuberculosis.

Smears for acid fast bacilli are only positive in 10–20% of Tuberculous effusions and are only 25–50% positive on pleural fluid culture.[8, 9] The addition of pleural biopsy histology and culture improves the diagnostic rate to about 90%.[9, 10]

Percutaneous pleural biopsies are of greatest value in the diagnosis of granulomatous and malignant disease of the pleura. They are performed on patients with undiagnosed exudative effusions, with non-diagnostic cytology, and a clinical suspicion of tuberculosis or malignancy. Occasionally, a blind pleural biopsy may be performed at the same time as the first pleural aspiration if clinical suspicion of tuberculosis is high.

Blind Percutaneous pleural biopsies

When using an Abrams' needle, at least four biopsy specimens should be taken from one site.

The Abrams' pleural biopsy needle is most commonly used in the UK with the Cope needle being less prevalent. At least four samples need to be taken to optimise diagnostic accuracy,[11] and these should be taken from one site as dual biopsy sites do

not increase positivity.[12] The biopsy specimens should be placed in 10% formaldehyde for histological examination and sterile saline for tuberculosis culture.

Complications of Abrams' pleural biopsy include site pain (1–15%), pneumothorax (3–15%), vasovagal reaction (1–5%), haemothorax (<2%), site haematoma (<1%), transient fever (<1%) and, very rarely, death secondary to haemorrhage. If a pneumothorax is caused, only 1% require chest drainage. [13, 14, 15-18]

In our series we used ABRAM"S pleural biopsy needle.

PLEURAL FLUID ANALYSIS:

Typical characteristics of the pleural fluid

The appearance of the pleural fluid and any odour should be noted.

A pleural fluid haematocrit is helpful in the diagnosis of haemothorax.

After performing pleural aspiration, the appearance and odour of the pleural fluid should be noted. The unpleasant aroma of anaerobic infection may guide antibiotic choice. The appearance can be divided into serous, blood tinged, frankly bloody, or purulent. If the pleural fluid is turbid or milky it should be centrifuged. If the

supernatant is clear, the turbid fluid was due to cell debris and empyema is likely. If it is still turbid, this is because of high lipid content and a chylothorax or pseudochylothorax is likely.[19]

Appearance of pleural fluid

Pleural Fluid	Suspected Disease
Putrid Odour	Anaerobic empyema
Food particles	Esophageal rupture
Bile stained	Chylothorax (biliary fistula)
Milky	Chylothorax/ pseudochylothorax
'Anchovy' sauce like fluid	Ruptured amoebic abscess

Key facts when investigating undiagnosed pleural effusions

If the pleural fluid protein is between 25 and 35 g/l, then Light's criteria are advised to differentiate accurately exudates from transudates.

Pleural fluid pH should be performed in all non-purulent effusions if infection is suspected.

When sending a pleural fluid specimen for microbiological examination, it should be sent in both a sterile tube (for Gram stain, AAFB and TB culture) and in blood culture bottles to increase the diagnostic yield.

Only 60% of malignant effusions can be diagnosed by cytological examination. A contrast enhanced CT scan of the thorax is best performed with the fluid present. This will enable better visualization of pleura and can identify the best site for pleural biopsy if cytological examination is unhelpful.

Grossly bloody pleural fluid is usually due to malignancy, pulmonary embolus with infarction, trauma, benign asbestos pleural effusions, or post-cardiac injury syndrome (PCIS).[20]

Differentiating between a pleural fluid exudate and transudate

The pleural protein should be measured to differentiate between a transudative and exudative pleural effusion. This will usually suffice if the patient's serum protein is normal and pleural protein is less than 25 g/l or more than 35 g/l. If not, Light's criteria should be used.

Light's criteria

The pleural fluid is an exudate if one or more of the following criteria are met:

Pleural fluid protein divided by serum protein >0.5

Pleural fluid LDH divided by serum LDH >0.6

Pleural fluid LDH more than two-thirds the upper limits of normal serum LDH

The classical way of separating a transudate from an exudate is by pleural fluid protein, with exudates having a protein level of >30 g/l and transudates a protein level of <30 g/l. A considerable number of other biochemical markers have been compared with Light's criteria. These include measuring pleural fluid cholesterol, albumin gradient, and serum/pleural fluid Bilirubin ratio.[21–25]

A cut off value of LDH levels in pleural fluid of >0.66, the upper limits of the laboratory normal might be a better discriminator ("Modified Light's criteria").[26]

The weakness of these criteria is that they occasionally identify an effusion in a patient with left ventricular failure on diuretics as an exudate. In this circumstance, clinical judgement should be used.

Differential cell counts on the pleural fluid

Pleural lymphocytosis is common in malignancy and tuberculosis.

Eosinophilic pleural effusions are not always benign.

When polymorphonuclear cells predominate, the patient has an acute process affecting the pleural surfaces. If there is concomitant parenchymal shadowing, the most likely diagnoses are Parapneumonic effusion and pulmonary embolism with infarction. If there is no parenchymal shadowing, more frequent diagnoses are pulmonary embolisms, viral infection, acute tuberculosis, or benign asbestos pleural effusion.[20, 27]

An eosinophilic pleural effusion is defined as the presence of 10% or more eosinophils in the pleural fluid. The presence of pleural fluid eosinophilia is of little use in the differential diagnosis of pleural effusions.[20] Benign aetiologies include parapneumonic effusions, tuberculosis, drug induced pleurisy, benign asbestos pleural effusions, Churg-Strauss syndrome, pulmonary infarction, and parasitic disease.[28-30] It is often the result of air or blood in the pleural cavity.[29]

If the pleural fluid differential cell count shows a predominant lymphocytosis, the most likely diagnoses are tuberculosis and malignancy. Although high lymphocyte counts in pleural fluid raise the possibility of tuberculous pleurisy,[20] as many as 10% of tuberculous pleural effusions are predominantly neutrophilic.[31] Lymphoma, sarcoidosis, rheumatoid disease, and chylothorax can cause a lymphocytic pleural effusion.[32]

pH

pH should be performed in all non-purulent effusions.

In an infected effusion a pH of <7.2 indicates the need for tube drainage. [33-34]

Glucose

A pleural glucose level of less than 3.3 mmol/l is found in exudative pleural effusions secondary to empyema, rheumatoid disease, lupus, tuberculosis, malignancy, or oesophageal rupture.[35] The lowest glucose concentrations are found in rheumatoid effusions and empyema.[35-37] In pleural infection, pH discriminates better than glucose.[34, 36] Rheumatoid arthritis is unlikely to be the cause of an effusion if the glucose level in the fluid is above 1.6 mmol/l (see section 8.6.1).[37]

Amylase

Amylase measurement should be requested if acute pancreatitis or rupture of the oesophagus is possible.

Iso-enzyme analysis is useful in differentiating high amylase levels secondary to malignancy or ruptured oesophagus from those raised in association with abdominal pathology.

Pleural fluid amylase levels are elevated if they are higher than the upper limits of normal for serum or the pleural fluid/serum ratio is >1.0.[38] This suggests acute Pancreatitis, pancreatic pseudocyst, rupture of the esophagus, ruptured ectopic pregnancy, or pleural malignancy (especially Adenocarcinoma).[20] Approximately 10% of malignant effusions have raised pleural amylase levels.[39]

Cytology

Malignant effusions can be diagnosed by pleural fluid cytology alone in only 60% of cases.

If the first pleural cytology specimen is negative, this should be repeated a second time.

If malignancy is suspected, cytological examination of the pleural fluid is a quick and minimally invasive way to obtain a diagnosis.[40-44]

Sensitivity of pleural fluid cytology in malignant pleural effusion

Reference	No. of Patients	No. Caused by Malignancy	% Diagnosed by Cytology
Salyer et al	271	95	72.6
Prakash et al	414	162	57.6
Nancy et al	385	109	71.0
Hirsch	300	117	53.8
Total	1370	371	61.6

The yield depends on the skill and interest of the cytologist and on tumour type, with a higher diagnostic rate for Adenocarcinoma than for mesothelioma, Squamous cell carcinoma, lymphoma and sarcoma.

Staining of pleural fluid:

A Gram stain of centrifuged pleural fluid should be obtained routinely. Smears of pleural fluid for AFB are positive in approximately in 20-30% of patients with Tuberculous pleurisy (American Thoracic Society).

Ultrasonogram

Ultrasound guided pleural aspiration should be used as a safe and accurate method of obtaining fluid if the effusion is small or loculated.

Fibrinous septations are better visualised on ultrasound than on CT scans.

Ultrasound is more accurate than plain chest radiography for estimating pleural fluid volume and aids thoracentesis.[45, 46]

Yang *et al*[47] found that pleural effusions with complex septated, complex non-septated, or homogeneously echogenic patterns are always exudates, whereas hypoechoic effusions can be either transudates or exudates. Ultrasound is also useful in demonstrating fibrinous loculation and readily differentiates between pleural fluid and pleural thickening.[48, 49]

Recently by using color Doppler it was observed that numerous echogenic floating particles within the pleural effusion (color signal), which is swirled in response to respiratory and cardiac cycle (this is fluid color sign)- is a sign of pleural effusion. None of the pleural thickening patient's shows fluid color sign (specificity 100%)

CT findings

CT scans for pleural effusion should be performed with contrast enhancement.

In cases of difficult drainage, CT scanning should be used to delineate the size and position of loculated effusions.

CT scanning can usually differentiate between benign and malignant pleural thickening.

There are features of contrast enhanced thoracic CT scanning which can help differentiate between benign and malignant disease Leung *et al*[50] showed that malignant disease is favoured by nodular pleural thickening, mediastinal pleural thickening, parietal pleural thickening greater than 1 cm, and circumferential pleural thickening. These features have specificities of 94%, 94%, 88%, and 100%, respectively, and sensitivities of 51%, 36%, 56% and 41%. When investigating a pleural effusion a contrast enhanced thoracic CT scan should be performed before full drainage of the fluid as pleural abnormalities will be better visualised.[51]

Recent advances in the diagnosis of pleural effusion:

The adenosine deaminase (ADA) level in pleural fluid tends to be higher with tuberculosis than in other exudates.[52, 53] However, ADA levels are also raised in empyema, rheumatoid pleurisy, and malignancy, which makes the test less useful in countries with a low prevalence of tuberculosis. Importantly, ADA levels may not be raised if the patient has HIV and tuberculosis.[54]

Adenosine deaminase (ADA) more than 70 IU/L (sensitivity 98%, specificity 96% in Tuberculous pleural effusion).

Others:

Concentration of glucose is higher than 60 mg/dl.

Needle biopsy shows 80% cases with demonstration of granuloma.

The level of ADA, lysozyme, leukocyte count, lymphocytes in Tuberculous effusion is higher than that of carcinomatous effusion.

Interferon-γ production in Tuberculous pleurisy is higher than that of malignant effusion.

Interleukin- 1, TNF-α also increased in Tuberculous effusion.

Tuberculous pleural effusion, detected by tuberculo-stearic acid in pleural aspirates. The sensitivity is 71 %(Grantham Hospital, Aberdin, Hong-Kong).

PCR in the diagnosis of Tuberculous pleural effusion is a G-C rich repetitive sequence (G=C RS) of Mycobacterium tuberculosis was identified in our Laboratory which displayed a high homology with amplification of the proximal 150 bp of G=C RS and its detection by non-radioactive hybridization was developed. The accuracy of G=C RS based PCR assay was evaluated in a clinical setting for the detection of Mycobacterial DNA in pleural fluids for the diagnosis of tuberculosis using clinical criteria and pleural biopsy histology as gold standard.

In a blind study, a total of 67 pleural fluid samples (38 Tuberculous and 29 Non-Tuberculous) were analyzed by PCR and the results were compared with pleural biopsy, Zeihl-Neihlson staining and culture.Mycobacteria could not be detected by either smear of culture techniques in any of the pleural fluid samples. Out of 38 Tuberculous pleural effusion, 24 were positive by PCR (63.2% histology, an increased sensitivity of 73.3% was obtained. Out of the obtained accounting for an overall specificity of 93.1%. G=C RS based PCR assay thus has a definite role in the diagnosis of Tuberculous Pleural effusion in contrast to smear/ culture techniques (AIIMS).

Thoracoscopy

Thoracoscopy should be considered when less invasive tests have failed to give a diagnosis.

Harris *et al*[55], Thoracoscopy over a 5 year period and showed it to have a diagnostic sensitivity of 95% for malignancy.

Bronchoscopy

Routine diagnostic bronchoscopy should not be performed for undiagnosed pleural effusion.

Bronchoscopy should be considered if there is haemoptysis or clinical features suggestive of bronchial obstruction.

Heaton and Roberts[56] bronchoscopy for undiagnosed pleural effusion. has a limited role in patients with an undiagnosed pleural effusion. It should be reserved for patients whose radiology suggests the presence of a mass, loss of volume or when there is a history of haemoptysis or possible aspiration of a foreign body.

Connective tissue diseases

Rheumatoid arthritis associated pleural effusions

Suspected cases should have a pleural fluid pH, glucose and complement measured.

Rheumatoid arthritis is unlikely to be the cause of an effusion if the glucose level in the fluid is above 1.6 mmol/l (29 mg/dl).

Measurement of C4 complement in pleural fluid may be of additional help, with levels below 0.04 g/l in all cases of rheumatoid pleural disease [108] Rheumatoid factor can be measured on the pleural fluid and often has a titre of >1:320

Systemic lupus erythematosis

The pleural fluid ANA level should not be measured as it mirrors serum levels and is therefore unhelpful.

The presence of LE cells in pleural fluid is diagnostic of SLE.[57, 58] Khare *et al*[111]

Pleural effusions in HIV infection

In patients with HIV infection, the differential diagnosis of pleural effusion is wide and differs from the immunocompetent patient.

A pleural effusion is seen in 7–27% of hospitalised patients with HIV infection. Its three leading causes are Kaposi's sarcoma, parapneumonic effusions, and tuberculosis.

EXAMINATION AND ANALYSIS OF

THE PLEURAL FLUID

EXAMINATION & ANALYSIS OF THE PLEURAL FLUID

1. Appearance:

Out of the 100 cases,

26 cases with pleural fluid were found to be **clear**

57 cases with pleural fluid were found to be **straw colored**

02 cases with pleural fluid were found to be **pus** and

15 cases with pleural fluid were found to be **hemorrhagic**

2. Pleural Fluid Protein:

In all the 20 transudative effusions, the pleural fluid protein is found to be less than 0.5 gm/dl

In all the 80 exudative effusions, the pleural fluid protein is found to be more than 3.5 gm/dl

In all the20 transudative effusions, the pleural fluid protein/serum protein is found to be less than 0.5

In all the 80 exudative effusions, the pleural fluid proteins/ serum protein is found to be more than 0.5

Note: The Light's Criteria states the ratio between pleural fluid to serum protein is more than 0.5. the ratio between pleural fluid LDH to serum LDH is more than 0.6.valdes et al described the ratio between pleural cholesterol to the serum cholesterol is more than 0.3(sensitivity 92.5%, specificity87.6%, it was found that with 0.4 as the cut of point, the specificity was 100%and sensitivity was 86.04%).

3. PLEURAL FLUID GLUCOSE:

In only two cases with pyogenic infections the pleural fluid glucose is less than 60 mg/dl.

4. PLEURAL FLUID AMYLASE:

In only two cases the pleural fluid amylase > 250 somogyi units/ l. The serum amylase was > 190 somogyi units/ l. the ratio between pleural fluid amylase and serum amylase is > 1.

5. GRAM'S STAINING:

In only one case the gram stain is found to be positive (Staph. aureus).

In all other cases gram stain was found to be negative.

6. PLEURAL FLUID CYTOLOGY:

Out of 100 cases in 8 cases, the pleural fluid cytology shows predominantly high polymorphonuclear leucocytes. In all the 15 hemorrhagic pleural effusion the erythrocyte count is more than 1000/cu.mm. In 10 cases of malignant pleural effusion the cytology for malignant cells were negative in 2 cases.

7. PLEURAL FLUID CULTURE:

In one patient with empyema the culture was positive for Proteus and in other it was positive for Staph.aureus.

8. PLEURAL BIOPSY:

In 6 cases positive for Tuberculous granuloma.

9. PLEURAL FLUID ADENOSINE DEAMINASE:

In 10 cases it was found to be positive > 70 IU.

10. EVIDENCES FOR TUBERCULOUS PLEURAL EFFUSION:

The Tuberculous etiology of pleural effusion is investigated and confirmed as follows,

* No. of cases with sputum AFB positive – 11

* No. of cases confirmed with pleural biopsy - 6

* No. of cases confirmed with ADA – 10

14 cases were found to be with definite past history of tuberculosis, having irregular treatment presented with pleural effusion. Also clinically, radiologically and paracentesis correlates with Tuberculous pleural effusion.

6 cases presented with pleural effusion gave history of contact with tuberculosis in their own family members like father/mother/wife.

In the rest of the cases were correlated clinically, radiologically and pleural fluid analysis. Further substantiated by their improvement with Anti-Tuberculous drug treatment (in the form of improvement in their appetite, gain in weight, regression of the pleural fluid on follow-up).

Since our resources and facilities are limited, we have not done culture for AFB, PCR, and Gammaferon. Tuberculosis is the commonest and more prevalent communicable disease in India, a straw colored fluid clots on standing with lymphocytes predominance itself will speak about the Tuberculous origin.

DISCUSSION

DISCUSSION

In our studies we studied 100 cases admitted for pleural effusion and we found that 67 cases were men and 33 cases were women.

INCIDENCE – AGE / SEX WISE

Total No. of cases	Male	Female
100	67	33

Age	Total no. of cases (%)	Male	Female
14-20	12(12%)	9	3
21-30	16(16%)	9	7

31-40	**10(10%)**	**7**	**3**
41-50	**26(26%)**	**17**	**9**
51-60	**13(13%)**	**7**	**6**
61-70	**14(14%)**	**12**	**2**
71-80	**06(6%)**	**5**	**1**
81 and above	**03(3%)**	**1**	**2**

Peak age incidence of pleural effusion is between 41-50 yrs (26%)

Constituents of Pleural Effusion:

	TRANSUDATE	**EXUDATE**
Nature of the fluid	clear	Straw colored, Turbid, Hemorrhagic
Protein	Less than 3 gm/dl	More than 3 gm/dl
Pleural Fluid/ serum Protein ratio	Less than 0.5	More than 0.5
Glucose	Same as Blood(+/-)	Low
Amylase	-	More than serum level (pancreatitis)
RBC	Less than 10,000/cu.mm	More than 1,00,000 Suggests neoplasm
WBC	Less than 1000/cu.mm	Usually over 1000cu.mm

Out of 100 cases 80 cases were exudates (80%) remaining 20 cases were transudates (20%)

Exudates:

Exudative causes	Cases	Percentage
Tuberculosis	66	66%
Malignancy	10	10%
Pyogenic	2	2%
Acute Pancreatitis	2	2%

Tuberculous pleural effusion:

In our study the incidence of Tuberculous effusion is common in males than females.

Sex wise incidence:

Total no. of cases	Male	Female
66	42	24

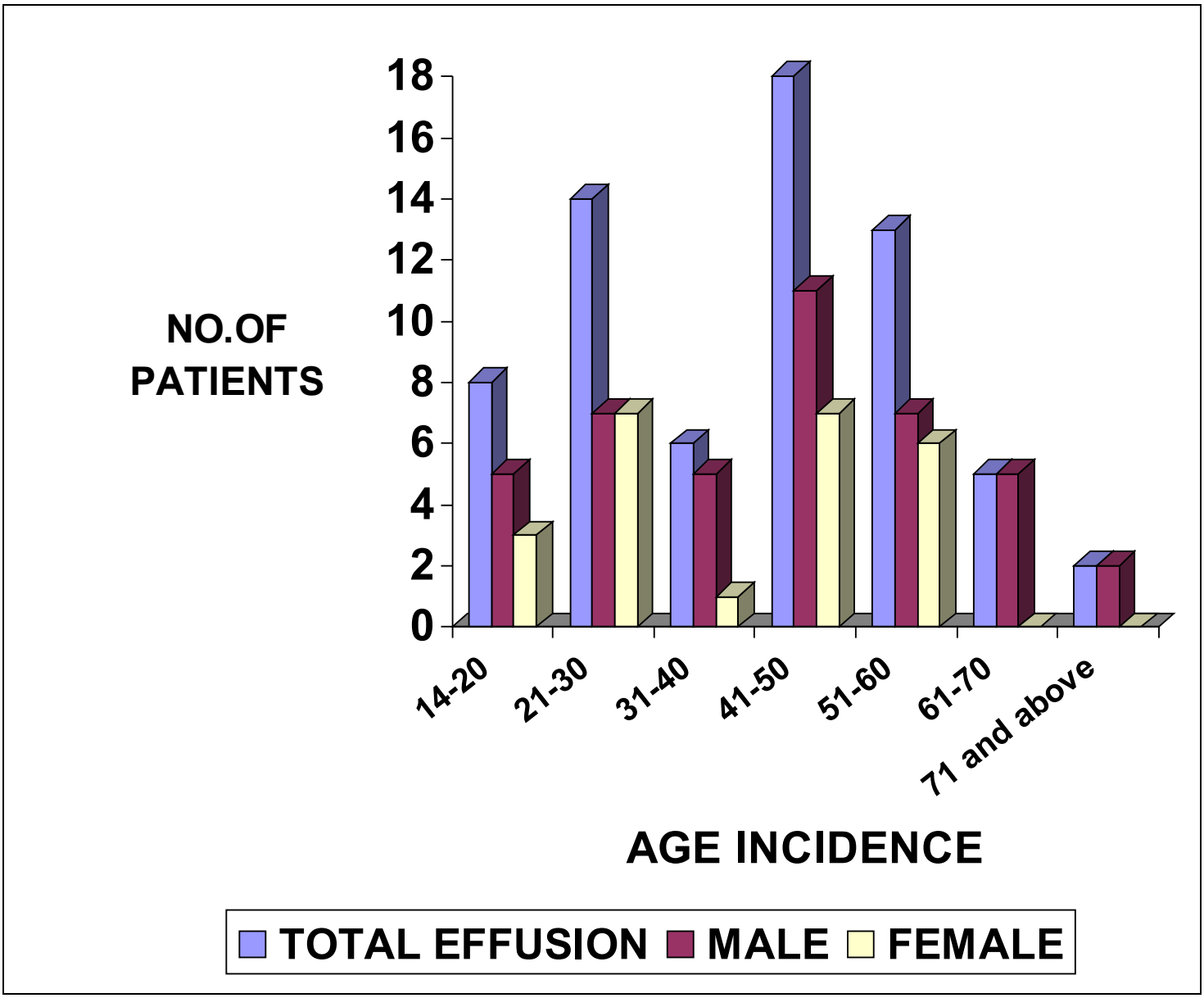
Age wise incidence:

Age	Total no. of TB Effusion	Male	Female
14-20	8	5	3
21-30	14	7	7
31-40	6	5	1
41-50*	18	11	7
51-60*	13	7	6

61-70	**5**	**5**	**0**
71 and above	**2**	**2**	**0**
Total	**66**	**42**	**24**

The peak age incidence of Tuberculous pleural effusion is between the age of 40-60 yrs in this Series

AGE INCIDENCE OF TUBERCULOUS PLEURAL EFFUSION



Risk Factors Related To Tuberculous pleural effusion

1. Past history of pulmonary tuberculosis present in 8/66 cases.
2. History of smoking present in 29/66 cases.

3. History of alcoholism present in 20/66 cases.
4. Diabetes mellitus present in 7/66 cases.
5. History of c\contact with pulmonary tuberculosis present in 6/66 cases.
6. All the 66 cases belong to low socio-economic group. We came to know that their dietary intake was very poor and their average monthly income was less than Rs.600/ month.

Clinical features:

Symptomatology of the patient:

Malaise, weight loss, and anorexia present in 59/66 cases.

Cough present in 64/66 cases.

Chest pain present in 50/66 cases.

Fever present in 63/66 cases.

Breathlessness present in 33/66 cases.

Hemoptysis present in 10/66 cases.

** 24 cases presented with anemia.

13 cases presented with clubbing

Mode of Presentation:

Acute	Sub acute	Chronic
12	44	16

Among the Tuberculous pleural effusion we studied right sided pleural effusion is more common than left sided pleural effusion and only two patients presented with B/L pleural effusion

Right	Left	Bilateral
47(31.02%)	16(10.56%)	3(1.98%)

Investigations

Sputum for AFB

11 patients were found to be positive.

Erythrocyte Sedimentation Rate (ESR):

ESR raised more than 30mm/ hr in all 66 cases. ESR was found to be >100mm/ hr in 5/66 cases.

Adenosine Deaminase (ADA):

10 cases investigated for ADA is positive for Tuberculous effusion. Value more than 70 IU.

Mantoux:

Negative in all cases.

Nature of the Pleural Fluid:

All the 66 cases were present with exudative effusion.

NATURE OF THE	NO. OF CASES

PLEURAL FLUID	
STRAW COLORED FLUID	**55**
FRANK PUS (EMPYEMA)	**6**
HAEMORRHAGIC	**5**
TOTAL	**66**

Pleural fluid protein / serum protein is more than 0.5 in all cases. Cells are predominantly lymphocytes. Polymorphs predominantly seen in Tuberculous empyema.

Radiological Presentation (associated pulmonary parenchymal lesions):

TB INFILTRATION			**FIBROSIS**			**CAVITY**		
Rt	**Lt**	**B/L**	**Rt**	**Lt**	**B/L**	**Rt**	**Lt**	**B/L**
11	**9**	**6**	**5**	**2**	**2**	**2**	**--**	**--**

- 4 cases presented with massive pleural effusion, 2 cases presented with loculated Pleural Effusion.

Pleural Biopsy:

We have done pleural biopsy only in selected no. of cases. 10 cases were subjected for pleural biopsy.

Biopsy Result:

Positive results for tuberculosis – 6 cases.

Non specific inflammation – 3 cases.

Only muscle tissue obtained – 1 case.

Echocardiography:

Only one patient 18/f presented with moderate pericardial effusion with Right sided pleural effusion. The pericardial effusion is detected by echocardiography.

E.C.G:

The above patient's ECG shows low voltage complexes.

C.T – Thorax:

CT lung done for two patient's shows loculated pleural effusion.

C.T – Brain:

Female aged 60 years presented with right sided pulmonary tuberculosis with synpneumonic effusion with convulsions. CT- brain shows tuberculoma in the right para-sagittal area in the posterior aspect of the parietal cortex.

MALIGNANT EFFUSION:

Out of 100 cases of pleural effusion malignant effusion was present in 10 cases (10%).

Primary neoplasm in the lung with Pleural Effusion 45 cases.

1) Squamous cell carcinoma, Rt. Lung – 2 cases, Lt. Lung – 2 cases.
2) Adenocarcinoma Lt. Lung – 2 cases, [illegible] ung – 2 cases.

Malignant effusion due to other causes –

1) Serous papillary cystadenocarcinoma of ovary.
2) Hodgkins Lymphoma – 1 case.

Malignant Pleural Effusion:

AGE	SEX	PRIMARY	NATURE OF EFFUSION	SITE OF EFFUSION	HISTOPATHOLOGICAL REPORT
84	**F**	Serous papillary cystadenocarcinoma of ovary	Hemorrhagic	Rt	Serous papillary cystadenocarcinoma
78	**M**	Mediastinal lymph node	Straw colored	Rt	Hodgkins lymphoma (lymphocytic depletion)
46	**M**	Lung	Hemorrhagic	Rt	Poorly differentiated Squamous cell carcinoma
70	**M**	Lung	Hemorrhagic	Lt	Papillary Adenocarcinoma
66	**M**	Lung	Hemorrhagic	Rt	Squamous cell carcinoma
62	**M**	Lung	Hemorrhagic	Lt	Well differentiated Squamous cell carcinoma
80	**M**	Lung	Hemorrhagic	Lt	Well differentiated Squamous cell carcinoma
48	**M**	Lung	Hemorrhagic	Rt	Papillary Adenocarcinoma
50	**M**	Lung	Hemorrhagic	Rt	Papillary Adenocarcinoma
60	**M**	Lung	Hemorrhagic	Lt	Papillary Adenocarcinoma

Clinical Presentation:

A female aged 84 yrs with serous papillary cyst Adenocarcinoma of ovary presented with lower abdominal pain and hemorrhagic pleural effusion on Rt. Side.

A 78 yrs female with Hodgkins lymphoma (lymphocytic depletion) presented with Rt. Side pleural effusion (straw colored) had lymph node enlargement in the cervical, inguinal and Mediastinal region,with fever, loss of weight, and appetite with breathlessness.

A 80 yrs female with poorly differentiated Squamous cell carcinoma presented with hemorrhagic massive Lt. Sided effusion with secondaries in the Lt. Supraclavicular node.

A 60 yrs male with Papillary Adenocarcinoma presented with massive hemorrhagic effusion on the Lt. Side with secondaries skull (Lt. temporal bone) involving petrous part sparing middle ear and extending into mastoid. This leads to LMN type of 7th cranial nerve palsy in the Lt. and 8th cranial nerve palsy on the Lt.

A 62 yrs male with hemorrhagic Rt. Sided pleural effusion with Squamous cell carcinoma of lung.

A 46 yrs male, a chronic smoker and diabetes with Rt. Side chest pain with massive hemoptysis associated with anemia had hemorrhagic Rt. Side pleural effusion diagnosed to have Well differentiated Squamous cell carcinoma.

A 70 yrs old male presented with breathlessness with chest pain and anemia with hemorrhagic pleural effusion on Lt. Side had well differentiated Adenocarcinoma.

A 66 yrs old male a chronic smoker and alcoholic with GTCS and features of hypercalcemia had multiple secondaries of brain had Hemorrhagic Rt. sided pleural effusion diagnosed to have Well differentiated Squamous cell carcinoma.

A 50 yrs male, a chronic smoker presented with Right sided chest pain with breathlessness and had a history of loss of appetite and loss of weight with Right sided hemorrhagic pleural effusion had well differentiated Adenocarcinoma.

A 48 yrs male presented with anorexia, hemoptysis, chest pain and exertional breathlessness had hemorrhagic Right sided pleural effusion. He was diagnosed to have well differentiated Adenocarcinoma.

EMPYEMA DUE TO PYOIGENIC INFECTION (2%):

A Female Aged 37 Yrs presented with fever, rigor, anorexia, had Lt. Side pyothorax. Thoracocentesis revealed frank pus predominantly containing polymorphs and her pleural fluid culture was positive for Proteus.

A male aged 19 yrs Rt. Sided chest pain with intercostals tenderness with high grade fever, rigor, chills, with breathlessness presented with Rt. Intercostals bulging diagnosed to have Rt. Sided massive pyothorax. Thoracocentesis revealed frank pus which predominantly contained polymorphs. His culture was positive for Staph. aureus.

ACUTE PANCREATITIS (2%):

A male aged 57 yrs presented with upper abdominal pain, vomiting, oliguria, dehydration, and hypotension had Lt. sided hemorrhagic pleural effusion. Pleural fluid Amylase was 350 S units/L. Serum Amylase is 200 S units/ L. The ratio of Pleural Fluid Amylase to Serum Amylase is > 1. the serum Calcium of this case is 8.2 mg %.

A 20 yrs male an alcoholic, smoker presented with hemetemesis and epigastric pain associated with hypotension and dehydration had Lt. sided pleural effusion. Pleural fluid Amylase was >300 S units/L. Serum Amylase is >200 S units/ L. The ratio of Pleural Fluid Amylase to Serum Amylase is > 1. The patients USG showed mild hepatomegaly.

TRANSUDATIVE PLEURAL EFFUSION:

20 cases out of 100 presented with transudative pleural effusion,

Transudative Causes	Cases	Percentage
Cardiac disease	15	15%

Renal disease	3	3%
Cirrhosis liver	2	2%

Pleural effusion due to cardiac diseases:

The commonest cause of transudative effusion in our study is due to cardiac failure. 15 out of 20 cases presented with feature of cardiac failure and pleural effusion. Among the 15 cases 11 presented with Rt. Side pleural effusion and 14 with Lt. sided pleural effusion.

The quantity of the pleural effusion is usually mild to moderate.8 cases were found to be males and 7 cases were found to be females.

AGE / SEX	RISK FACTORS	CAUSE OF CARDIAC FAILURE	CLINICAL PRESENTATION
37 / M	Smoking	Ischemic heart disease (old extensive anterior wall myocardial infarction)	Congestive cardiac failure with right sided pleural effusion
30 / M	Nil	Old antero-septal myocardial infarction	Congestive cardiac failure with right sided pleural effusion
43 / M	Smoking Alcoholism	High lateral wall ischemia	Left ventricular failure with right sided pleural effusion
44 / M	Smoking Alcoholism and Tobacco chewing	Non- Q anterior wall myocardial infarction	Congestive cardiac failure with right sided pleural effusion
68 / M	Smoking	Old inferior wall myocardial infarction	Left ventricular failure with right sided pleural effusion

61 / M	Smoking Alcoholism	Antero-lateral ischemia	Congestive cardiac failure with left sided pleural effusion
66 / F	Nil	Antero-septal myocardial infarction	Congestive cardiac failure with right sided pleural effusion
50 / F	Nil	Old inferior wall myocardial infarction with right ventricular myocardial infarction	Congestive cardiac failure with right sided pleural effusion
70 / M	Smoking	Antero-septal myocardial infarction with Left Bundle Branch Block	Congestive cardiac failure with right sided pleural effusion
49 / F	Tobacco chewing	High lateral wall ischemia	Congestive cardiac failure with left sided pleural effusion
74 / F	Nil	Inferior wall Myocardial Infarction with RVMI	Congestive cardiac failure with left sided pleural effusion
81 / F	Smoking Alcoholism and Tobacco chewing	Antero-septal myocardial infarction	Congestive cardiac failure with left sided pleural effusion
66 / F	Nil	Old Antero-septal myocardial infarction	Congestive cardiac failure with right sided pleural effusion
43 / M	Nil	Infe[56]ral wall Ischemia	Congestive cardiac failure with right sided pleural effusion
38/F	Nil	Infero-lateral wall Ischemia	Congestive cardiac failure with right sided pleural effusion

Common symptoms:

1) Breathlessness

2) Paroxysmal nocturnal dyspnoea

3) Orthopnoea

4) Cough

5) Angina type of chest pain

Signs:

1) Pedal edema present ion all 15 cases
2) JVP elevated in all 15 cases
3) Cardiomegaly present in all 15 cases
4) LV S3 – gallop present in 8 cases
5) Short systolic murmur due to MR present in 3 cases
6) Basal crepts present in all 15 cases
7) Tender hepatomegaly present in 12 cases
8) Free fluid in the abdomen present in 8 cases

ECG shows evidence for old infarction as well as ischemia in all 15 cases.

X- Ray chest PA view shows Cardiomegaly present in all 14 cases. CT ratio > 0.5 in all 15 Cases.

Echocardiography shows dilated heart with severe Left ventricular dysfunction in all 15 cases.

In only 3 cases there was mild MR (Mitral regurgitation) secondary to LV dysfunction.

TRANSUDATIVE EFFUSION DUE TO RENAL DISEASE (4 CASES):

1) Nephrotic syndrome(1 cases):

A 19 yr old boy, presented with puffiness of face and generalized edema and dyspnoea, with Right sided pleural effusion and his 24 Hr urinary protein is > 3.6

gms. Serum protein is 5 gm/dl. Pleural fluid protein is 0.5 gm/ dl. And urine albumin is + +++.

2) A 71 yr old Male, a known diabetic and hypertensive diagnosed as diabetic nephropathy with CRF presented with B/L pleural effusion.

3) A 39 yr old female, presented with breathlessness, puffiness of face, B/L pedal edema, oliguria and anorexia. The patient was found to have Diabetes Mellitus for 8 yrs and systemic hypertension for 6 months.

24 Hrs urinary protein is > 3.6 gms, blood urea is 80 mgs, serum creatinine is 3.5 mgs%. Serum potassium 6.2 mEq/L.

USG – abdomen shows B/L pleural effusion with Grade-1 medical renal disease.

X – Ray chest PA view shows B/L pleural effusion.

PLEURAL EFFUSION DUE TO CIRRHOSIS LIVER WITH PORTAL HYPERTENSION (2 CASES):

A 84 yr old male presented with abdominal distention, hemetemesis and breathlessness. The patient was found to have jaundice before 5 yrs. The patient was a smoker and alcoholic for 25 yrs. Clinically the patient presented with Grade- 2 clubbing. Edema in both foot, abdominal distention, engorged veins seen over the abdominal flanks and the blood flow is below upwards. Mild spleenomegaly present. Liver function tests shows hypoalbuminemia. Albumin: globulin reversed. X- Ray chest shows right sided pleural effusion. Pleural aspirate is clear and transudative. USG- abdomen shows

increased liver echogenicity. Portal vein diameter is 14 mm. spleen is enlarged. Hepatic segment of the inferior venacava is narrowed. Sub hepatic renal segment dilated and blood flow is sluggish.

A 19 yr old male presented with abdominal distention, hemetemesis, loss of appetite, nausea, vomiting, melena and breathlessness.. Patient presented with jaundice, Puffiness of face, abdominal distention, Edema in both foot. Engorged veins seen over the abdominal flanks. Massive ascites is present. Mild spleenomegaly present. Liver function tests shows hypoalbuminemia. Serum bilirubin > 6 mg%. SGOT- 180U, SGPT – 220U, HBsAg- negative. Urinary bile salt and bile pigment positive. Albumin: globulin reversed. X- Ray chest shows right sided pleural effusion. Pleural aspirate is clear and transudative. USG- abdomen shows nodular shrunken liver with increased echogenicity. Portal vein diameter is 18 mm. Mild spleenomegaly present.

RESOLUTION OF PLEURAL EFFUSION[78]

Diseases	Incidence, %	Therapy	Resolution Time (Range)
Parapneumonic effusion (unc)			
Non-HIV	40–90	Antibiotics	2–8 wk
HIV positive	21	Antibiotics	2–3 wk
Tuberculosis			
Non-HIV	3–23	No therapy	2–4 mo
		INH, rifampin	
		INH, rifampin, PZA	1–2 mo
		Addition of prednisone	1–2 mo
HIV positive	3–40	INH, rifampin, PZA	1–2 mo
CHF	40–60	Diuretics, ACE-I, digoxin	< 1 mo
PCIS			
Post myocardial infarction	40–68	NSAIDs; prednisone	1–5 wk (1 wk–4 mo)

Postpericardiotomy	41–85	NSAIDs; prednisone	1–3 wk (1 wk–4 mo)
Postcoronary artery bypass	40–90	Self-limited	8 wk (6 wk–20 mo)
RA	4–7	Nonsteroidals; prednisone	3–4 mo (1 mo–5 yr)
SLE	16–37	Corticosteroids	2 wk (1–6 wk)
Sarcoidosis	0–7.5	Self-limited; prednisone	1–3 mo (2 wk–6 mo)
Pulmonary embolism	10–50	Heparin; LMWH	< 1 wk (3–7 d)
Benign asbestos effusion	1–9	Self-limited	3–4 mo (1–17 mo)
After organ transplantation			
Lung and heart-lung	100	Self-limited	
Liver	50–100	Self-limited	2–3 wk (3 d–7 mo)
Uremia	2–3	Hemodialysis	4–6 wk
Pancreatitis			
Acute	4–20	Treat acute pancreatitis	2 wk (1–8 wk)
Chronic	5	NPO; TPN; thoracentesis	2–3 wk (1–8 wk)

ACE = Angiotensin-Converting Enzyme Inhibitor; INH = Isoniazid; LMWH = Low-Molecular-Weight heparin; PZA = Pyrazinamide; TPN = Total Parenteral Nutrition; unc = Uncomplicated; NPO = Nothing by mouth

SUMMARY

SUMMARY

In Our Study 100 cases of pleural effusion were taken up and we found that the incidence is more common in males than in females.

It has been found that Tuberculosis is the most common cause of pleural effusion as it is the most prevalent infectious disease in India. Out of the 100 cases 66 patients were to be of Tuberculous etiology.

Tuberculous pleural effusion with clinical presentation (66 cases, 66%)

Out of 66 cases of Tuberculous pleural effusion majority of cases were presented with the following manifestations like cough with expectoration, sputum, chest pain,

fever, loss of appetite and loss of weight. Apart from the above Symptomatology, dyspnoea and hemoptysis were present.

Malignant Effusion (10 cases, 10 %):

Out of 10 neoplastic conditions eight presented with effusion primarily of lung pathology in the form of Adenocarcinoma and Squamous cell carcinoma. The patient with Squamous cell carcinoma presented with cough, chest pain, hemoptysis, dyspnoea, clubbing and enlarged Left Supraclavicular node. The Adenocarcinoma patient apart from the above symptoms also presented with secondaries in the skull and facial palsy and deafness.

The other 2 were found to be serous papillary cystadenocarcinoma of ovary and Hodgkins lymphoma (1 case).

The patient with serous papillary cystadenocarcinoma of ovary presented as painful lower abdominal lump..

The patient with Hodgkins lymphoma (1 case) presented with symptoms of Mediastinal mass with chest pain and breathlessness other one presented with generalized lymphadenopathy, fever and weight loss.

Cardiac failure with pleural effusion (15 cases, 15%):

All cases were due to post infarction failure. They presented with symptoms of anginal chest pain, palpitation, paroxysmal nocturnal dyspnoea, Orthopnoea and cough.

Pleural Effusion Due To Renal Disease (3 cases, 3%):

Nephrotic Syndrome with Pleural Effusion (1 case):

The patient presented with puffiness of face, generalized edema, dyspnoea and cough.

Diabetic nephropathy with pleural effusion (2 cases):

Diabetic nephropathy leading on to chronic renal failure presented with easy fatigability, puffiness of face, oliguria, volume overload and dyspnoea.

Cirrhosis with pleural effusion (2 cases):

The patient presented with abdominal distention hemetemesis, B/L pedal edema, oliguria, loss of appetite and other evidence of portal hypertension.

Acute Pancreatitis (2 cases):

`Patient presented with acute abdominal pain, vomiting, hemetemesis, dehydration and hypovolemic shock.

Pyogenic effusion (2 cases):

Both patients presented with high grade fever associated with rigor and chills, dyspnoea and the patient was found to be toxic and delirious. The pus cultures were positive for Proteus in one and Staph. aureus in the other.

Study done by Govindasamy et al., 1985 shows 73.3% Tuberculous pleural effusion, 16.7% due to malignant pleural effusion, 6.7% were due to cardiovascular disease and 3.3% were due to liver disease.

In our series, etiological causes of pleural effusion are as follows:

66% due to Tuberculosis

10% due to Malignancy

15% due to Cardiac disease

3% due to Renal disease

2% due to Pyogenic effusion

2% due to Acute pancreatitis

2% due to Liver disease

According to Harrison's principles of internal Medicine 16th edition 2005, the most commonest cause of pleural effusion in cardiac disease is Left ventricular failure. In our study also all the Fifteen cardiac disease patients with pleural effusion are due to Left ventricular failure.

According to Oxford Text Book of Medicine, 4th edition 2003, in acute pancreatitis with pleural effusion the ratio between pleural fluid Amylase/ serum amylase > 1. in our study also acute pancreatitis with pleural effusion, the ratio of pleural fluid amylase 350 S units/L / serum amylase 200 S units/L is > 1.

CONCLUSION

CONCLUSION

100 patients admitted in medical wards of Coimbatore Medical College Hospital, Coimbatore, with pleural effusion were investigated and the following conclusions were drawn:

66% due to Tuberculosis

10% due to Malignancy

15% due to Cardiac disease

3% due to Renal disease

2% due to Pyogenic effusion

2% due to Acute pancreatitis

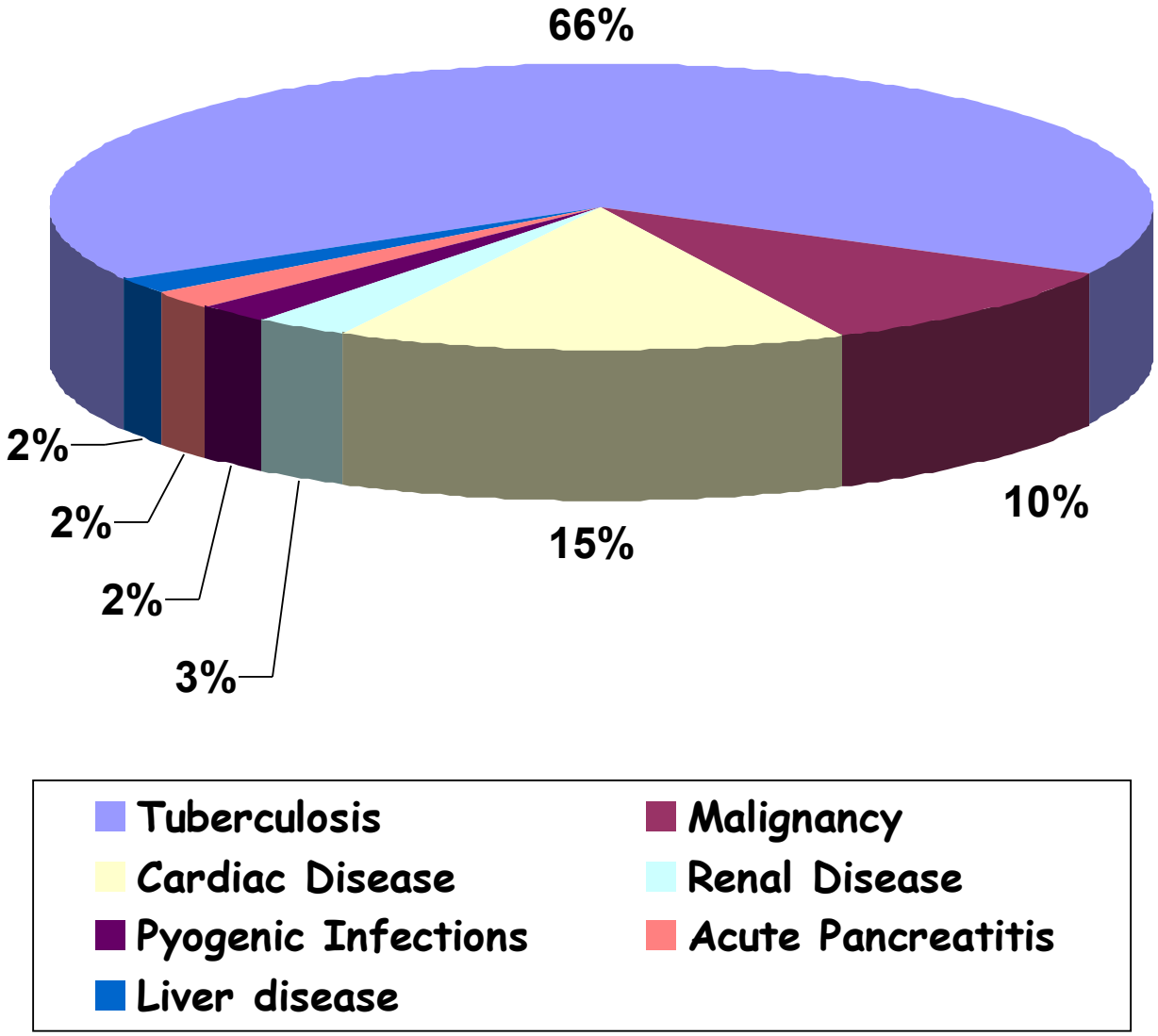
2% due to Liver disease

Peak age incidence of pleural effusion is between 41 – 50 years the peak age incidence of Tuberculous pleural effusion is between 40 – 60 years. **The commonest cause was found to be Tuberculosis.**

Rare causes of pleural effusion were found to be:

1) acute pancreatitis with pleural effusion
2) papillary serous cystadenocarcinoma of ovary with pleural effusion
3) Hodgkin's lymphoma (lymphocyte depletion) with pleural effusion.

ETIOLOGICAL DIAGNOSIS OF PLEURAL EFFUSION



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PROFORMA

AETIOLOGICAL DIAGNOSIS IN PLEURAL EFFUSION

PROFORMA

Name: **Age:** **Sex:**

Address: **Occupation:** **DOA:** **DOD:**

<u>COMPLAINTS WITH DURATION:</u>

Cough

Expectoration

Dyspnoea

Chest pain

Change of voice

Oedema

Malaise or weight loss

Fever

PAST HISTORY:

H/o similar episodes:

Contact with known TB patient:

Diabetes mellitus:

Hypertension:

Sexually transmitted diseases:

H/o Asthma:

H/o Allergy to drug:

H/o Aspiration, head injury, epilepsy, coma, convulsion, alcohol, general anaesthesia, recurrent resp. tract infection, drug intake, corrosives.

TREATMNT HISTROY:

IV fluid therapy:

Injections and admission to the hospital:

FAMILY HISTORY:

Similar episodes in the family:

H/o consanguineous marriage, bronchiectasis:

No: of children:

PERSONAL HISTORY:

Smoker, alcoholic, diet, sleep rhythm.

SOCIO-ECONOMIC STATUS:

MENSTRAL H/o:

Menarche, periods regular, 3/30:

Last menstrual period:

<u>GENERAL EXAMINATION:</u>

Built

Nourishment

Consciousness

Orientation

Febrile/ Afebrile

Anaemia

Jaundice

Cyanosis

Clubbing

Pedal edema

Generalized lymphadenopathy

Bony abnormality

Spinal deformity

Scrofuloderma

Horner's syndrome

Erythema nodosum

Sinuses

Scar

<u>VITAL SIGNS:</u>

Pulse: ……. / min, Bp: …….mmHg, Resp. rate: ……./min,

Temp: ……0C, **Heart rate: ……/ min.**

EXAMINATION OF THE UPPER RESPIRATORY SYSTEM:

Sinusitis, Deviated nasal septum, Rhinorrhoea, Oral hygiene,

Tonsillitis, pharyngitis, Odour of the breath.

EXAMINATION OF LOWER RESPIRATORY SYSTEM:

INSPECTION:

- **Position of the trachea** **left / mid / right**
- **Apical impulse**
- **Shape of the chest wall** **symmetry / asymmetry**
- **Move of the chest wall** **symmetry / asymmetry**
- **Equal on both sides** **Diminished Rt / Lt**

- **Movement of the diaphragm**
- **Movement of the scapula**
- **Accessory muscles of the respiration**
- **Supra clavicular hollowing / fullness**
- **Infra clavicular hollowing / fullness**
- **Drooping of the shoulder Rt / Lt**
- **Inter costal indrawing / bulging**
- **Precordial bulge**
- **Engorged veins**
- **Spinal deformity: kyphosis / scoliosis / lordosis.**
- **Sternal deformity: pectus carinatum /pectus excavatum**

- **Presence of any sinus or scars**

- **Scapular region: winging / fullness**

- **Traube's space fullness**

- **JVP**

<u>PALPATION:</u>

- **Trachea**

- **Apical impulse**

- **Size of the chest insp / exp**

- **Shape on expansion symmetry / asymmetry**

- **Intercostal tenderness**

- **Tactile fremitus: rhonchi / rales**

- **Vocal fremitus**

<u>PERCUSSION:</u>

Anterior

- **Percussion over the clavicle**

- **Apical supraclavicular area**

- **Kronig's band of resonance**

- **Clavicle Rt / Lt**

- **Infraclavicular area Rt / Lt**

- **Mammary area: supra Rt / Lt**

  Infra Rt / Lt

- **Intercostal space Rt / Lt**

- **Liver dullness**

Posterior

- **Supra scapular** **Rt / Lt**
- **Inter scapular** **Rt / Lt**
- **Infra scapular** **Rt / Lt**

Lateral

- **Axilla** **Rt / Lt**
- **Infra axillary area** **Rt Lt**

Shifting dullness **Rt / Lt**

Sound of coin **Rt / Lt**

Straight line dullness

Cardiac dullness

Traube's space obliteration

<u>AUSCULTATION:</u>

- **Breath sounds**

  - **Vesicular / bronchial**

    High / low

    Tubular / cavernous /

    Amphoric

- **Post tussive suction**

- **Coin test**

- **Whispering pectoriloqy**

- **Bronchophony**

- **Aegophony**

- **Added Sounds:**

  - Pleural rub insp exp both

  - Crepitation fine course

  - Wheeze monophonic polyphonic

  - Rhonchi

    - rales

    - succusion splash

    - coin test

- post tussive suction rale

- **Vocal resonance**

OTHER SYSTEM EXAMINTION

Cardio-vascular system

Abdomen

Central nervous system